REMARKS

The present application was filed on December 5, 2001 having claims 1-84. Claims 17-22, 38-72 and 75-84 are cancelled herein as being drawn to a non-elected invention. Thus, Claims 1-6, 23-37, and 73-74 are pending in the application.

In the Office Action dated January 5, 2004, the Examiner: (1) rejected Claims 1-6 and 73 under 35 U.S.C. §112, second paragraph, as being indefinite; (2) rejected Claims 1, 2, 5, 6 and 73 under 35 U.S.C §102(b) as anticipated by WO 91/07505 to Hornes et al. ("Hornes"); and rejected Claims 1-6, 23-32, 37, 73 and 74 under 35 U.S.C §102(e) as anticipated by U.S. Patent No. 6,610,742 to Zhu et al. ("Zhu").

With respect to the rejection of Claims 1-6 and 73 under 35 U.S.C. §112, second paragraph, the language in question was "the second portion...being at least 20 nucleotides removed from the first portion..." The term "removed" is used in its ordinary sense. While the dictionary includes several definitions of removed, taking applicants' specification into consideration, it is clear that the relevant dictionary definition of "removed" in the present situation is "separated or remote in space, time or character". While applicants respectfully submit the original claim language was sufficiently clear, in the interests of advancing prosecution, Claims 1-5 have been amended to recite that the second portion of a nucleic acid encoding a polypeptide is separated by at least 20 nucleotides from a first portion (claim 1), which can be in the 5' direction (claim 5). Applicants respectfully submit that the scope of the claims is unchanged and that no new matter has been added as a result of this amendment. Reconsideration of this rejection is thus respectfully requested.

With respect to the rejection of Claims 1, 2, 5, 6 and 73 under 35 U.S.C §102(b) as anticipated by Hornes, this rejection is respectfully traversed.

Nowhere does Hornes disclose or suggest a plasmid having a primer sequence incorporated into the plasmid, the primer sequence being capable of annealing to a first portion of nucleic acid encoding a polypeptide, and a collar sequence incorporated into the plasmid, the

collar sequence being capable of annealing to a second portion of the nucleic acid encoding the polypeptide, as required by amended Claim 1.

Although it is alleged in the Office Action that Hornes discloses that regions of homology can be present in the target nucleic acid, nowhere does Hornes disclose incorporating the regions of homology into the plasmid as presently recited in Claim 1. The plasmids of the present disclosure are engineered to contain two template annealing sequences, namely a downstream primer sequence capable of annealing to a first portion of a nucleic acid encoding a polypeptide, and an upstream collar sequence capable of annealing to a second portion of said nucleic acid encoding a polypeptide. (See Applicants' specification at page 3, lines 3-9.) It is not seen where in the Hornes reference there is any disclosure of modifying a plasmid to arrive at the presently claimed plasmid. Therefore, in view of the foregoing amendment and remarks, reconsideration of the rejection of Claims 1, 2, 5, 6 and 73 as anticipated by Holmes is respectfully requested.

Claims 1-6, 23-32, 37, 73 and 74 were rejected under 35 U.S.C §102(e) as anticipated by Zhu. This rejection is also respectfully traversed.

Nowhere does Zhu disclose or suggest a plasmid having a primer sequence incorporated into the plasmid, the primer sequence being capable of annealing to a first portion of nucleic acid encoding a polypeptide, and a collar sequence incorporated into the plasmid, the collar sequence being capable of annealing to a second portion of the nucleic acid encoding the polypeptide, as presently recited in Claim 1.

In fact, as with Hornes, the region of homology of Zhu is placed in the target peptide or antibody, not incorporated into the plasmid. Zhu specifically discusses the process for engineering its target peptide to facilitate recombination with a plasmid at column 29, lines 10-34:

> By using homologous recombination in yeast, gene fragments or synthetic oligonucleotides can also be cloned into a plasmid vector without a ligation step. In this application, a targeted gene fragment is usually obtained by PCR amplification (or by using the conventional restriction digestion out of an original cloning vector). Two short fragment sequences

> ***that are homologous to the plasmid vector are added to the 5' and 3' of the target gene fragment*** in the PCR amplification. This can be achieved by using a pair of PCR primers that incorporate the added sequences... The linearized plasmid vector and the target gene fragment flanked by sequences homologous to the plasmid vector are co-transformed into a yeast host strain. The yeast recognizes the two stretches of sequence homologies between the vector and target fragment, and facilitates a reciprocal exchange of DNA contents through homologous recombination at the gap. As the consequence, the target fragment is automatically inserted into the vector without ligation in vitro.

While Zhu teaches that its methods may be utilized to incorporate heavy chain regions of an antibody (V1) and light chain regions of an antibody (V2), the process for incorporating these two regions into a plasmid clearly require providing the V1 and V2 regions with flanking sequences that are homologous to the plasmid; Zhu does not insert primer or collar sequences into the plasmid. Zhu provides great detail as to its method at column 30, lines 27-64, which requires

> a) transforming into yeast cells i) a linearized yeast expression vector having a 5'- and 3'-terminus sequence at a first site of linearization; and ii) a library of first insert nucleotide sequences that are linear, double stranded, each of the first insert sequences comprising a first nucleotide sequence V1 encoding a first polypeptide subunit, a 5'- and 3'-flanking sequence at the ends of the first insert sequence which are sufficiently homologous to the 5'- and 3'-terminus sequences of the vector at the first site of linearization, respectively, to enable homologous recombination to occur;
>
> b) having homologous recombination occur between the vector and the irst [sic] insert sequence in the transformed yeast cells, such that the first insert equence [sic] is included in the vector;
>
> c) isolating from the transformed yeast cells the vectors that contain the library of the first insert sequences;
>
> d) linearizing the vectors containing the library of the first insert sequences

to generate a 5'- and 3'-terminus sequence at a second site of linearization;

e) transforming into yeast cells

i) the linearized yeast expression vectors in step d), and

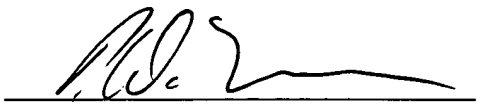
ii) a library of second insert nucleotide sequences that are linear, double stranded, each of the second insert sequences comprising a second nucleotide sequence V2 encoding a second polypeptide subunit, a 5'- and 3'-flanking sequence at the ends of the second insert sequence which are sufficiently homologous to the 5'- and 3'-terminus sequences of the vector at the second site of linearization, respectively, to enable homologous recombination to occur; and

f) having homologous recombination occur between the linearized yeast expression vector at the second linearization site and the second insert sequences in the transformed yeast cells, such that the second insert sequence is included in the vector.

As the primer and collar sequences of Claim 1 are engineered into a plasmid, and such modification of the plasmid is nowhere taught or suggested by Zhu, reconsideration of the foregoing rejection is respectfully requested.

It is believed that the claims of the application as now presented, i.e., Claims 1-6, 23-37, and 73-74, are patentably distinct over the art of record and are in condition for allowance. In the event that the examiner believes that a telephone conference or a personal interview may facilitate resolution of any remaining matters, the undersigned may be contacted at the number indicated below. In view of the foregoing amendment and remarks, early and favorable reconsideration of this application is respectfully requested.

Respectfully submitted,



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